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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,866	07/02/2002	Michael Schirner	SCH 1869	6769

23599 7590 02/18/2005

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EXAMINER	
HUFF, SHEELA JITENDRA	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 02/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,866	SCHIRNER ET AL.	
	Examiner	Art Unit	
	Sheela J Huff	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-14 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-14 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-14 are pending.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The IDS filed 9/6/02 has been made of record and an initialed copy of the PTO-1449 is enclosed. The material that is crossed off appears to refer to page no. 0f the above references.

SSH

Specification

The disclosure is objected to because of the following informalities: On page 5, line 5, the specification says that E8 is disclosed by Viti et al. Viti et al discloses E1 not E8..

Appropriate correction is required.

Claim Rejections - 35 USC § 112/101

Claims 11-14 provide for the use of the antibody-conjugate, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 11-14 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Regarding claims 4 and 14, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

b. Regarding claim 1, the phrase "preferably" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

c. In claim 5, "dye-$(F)_n$" renders the claim vague and indefinite. "Dye-$(F)_n$" refers to claim 1, and in claim 1 the formula is "B-$(F)_n$" where B is the antibody and F is the dye. There is no proper antecedent basis for "dye-$(F)_n$" which is a dye-dye conjugate.

d. In claim 5, the terminology "and/or" renders the claim vague and indefinite. It should be either --and-- or --or--.

e. In claim 11, the terminology "and agents" lacks proper antecedent basis.

f. In claim 13 it is not clear what "microscopic and macroscopic intraoperative visualization" means. Is applicant using a microscope?

Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials.

The specification lacks complete deposit information for the deposit of hybridoma cell lines producing L19 and E8. It is not clear that hybridomas possessing the identical properties of the aforementioned hybridomas are known and publicly available or can be reproducibly isolated from nature without undue experimentation.

Exact replication of a cell line is an unpredictable event. Although applicant has provided a written description of a method for selecting the claimed hybridoma cell lines and monoclonal antibodies, this method will not necessarily reproduce antibodies and hybridomas which are chemically and structurally identical to those claimed. It is unclear that one of skill in the art could derive a monoclonal antibody and hybridoma identical to those claimed. Undue experimentation would be required to screen all of the possible antibody and hybridoma species to obtain the claimed antibodies and hybridomas.

Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed monoclonal antibodies, a suitable deposit for patent purposes, evidence of public availability of the claimed L19 and E8 or evidence of the reproducibility without undue experimentation of the claimed antibodies, is required.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made

under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit is not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 and 8-10 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Neri et al Nature Biotechnology Vol. 15 p. 1271 (11/97).

This reference discloses making and using scFv(CGS-1) labeled with infrared fluorophore CY and the use of this antibody-dye conjugate to detect blood vessels and to image tumors (reads on using in a pharmaceutical composition) in tumors by fluorescence microscopy (see page 1272 and 1273). ScFv is directed to ED-B fibronectin, which as is also known as oncofetal fibronectin (see abstract). It is inherent that the conjugate "accumulates in the edge area of the cell tissue of a focus of disease" making the edge area of the focus of disease optically detectable.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 and 7-10 and 14 rejected under 35 U.S.C. 103(a) as being unpatentable over Neri et al Nature Biotechnology Vol. 15 p. 1271 (11/97) in view of applicant's admission on page 2, line 20-21 and page 8, line 13 to page 9, line 16 of the specification.

Neri et al has been discussed above.

The only difference between the instant invention and the reference is the use of the different dyes.

On pages 2 and 8-9 of the specification, applicant admits that "dyes for the visualization of foci of disease are already known" and on pages 8-9 lists a wide variety of known dyes.

Since the antibody-dye conjugates of the primary reference are used to image tumors, and since many dyes for the visualization of disease are already known in the art, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use the known dyes in the antibody-dye conjugate of the primary reference with the expected benefit of imaging a tumor.

Claims 1-2, 6 and 8-10 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neri et al Nature Biotechnology Vol. 15 p. 1271 (11/97) in view of Viti et al Cancer Research vol. 59 p. 347 (1/99).

Neri et al has been discussed above.

The only difference between the instant invention and the reference is the use of antibody L19.

Viti et al discloses that antibody L19 can be used in vivo to target new forming blood vessels of F9 teratocarcimona(page 349 (second column)) and that these antibodies have increased binding affinity.

In view of the fact that L19 can target newly formed blood vessels in vivo and has increased binding affinity, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use L19 in the conjugate of the primary reference with the expected benefit of achieving an antibody-dye conjugate with higher binding affinity.

Claims 1-2, 5 and 8-10 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neri et al Nature Biotechnology Vol. 15 p. 1271 (11/97) in view of Licha et al US 6083485 (filed 11/7/97)

Neri et al has been discussed above.

The only difference between the instant invention and the reference is the cyanine dyes of claim 5.

Licha et al disclose a protein-dye conjugate wherein the dye is "F" (col. 4-5) and the a cyanine dye of the formula IIa. This formula reads on applicant's formula in claim 5. The dyes of this reference are based on near infrared radiation and used in vivo in diagnostic methods and this is accomplished by recording the fluorescent radiation produced from the cyanine dye (see abstract and claims).

Since Licha et al discloses protein-dye conjugates using cyanine dyes and the use of these dyes in in vivo diagnostics, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use the dyes of the secondary reference in place of the dyes of the primary reference with the expected benefit of achieving a conjugate that can be used in vivo diagnostic assays.

Claims 1 and 11-12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neri et al Nature Biotechnology Vol. 15 p. 1271 (11/97) in view of Poon et al J. Neurosurg. Vol. 76 p. 685 (1992).

Neri et al has been discussed above.

The only difference between the instant invention and the reference is the intraoperative visualization or for microscopic and macroscopic intraoperative visualization of foci of disease.

Poon et al discloses a fluorescence system using a fluorescent label in vivo and "the use of laser-induced fluorescence to increase the accuracy with which rat brain-tumor margins are defined (p. 684-second column-Discussion) and that this system could easily be applied to surgery and the identification of tumor resection margins (p. 685 (first column).

In view of the fact that Poon et al shows the use of a fluorescent label to increase the accuracy with which rat brain-tumor margins are defined it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to replace the label of the primary reference with the label of Poon et al with the expected benefit of using the resulting conjugate to define the margins of brain-tumors.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J Huff whose telephone number is 571-272-

0834. The examiner can normally be reached on Mondays and Thursdays from 5:30am to 2:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheela J Huff
Primary Examiner
Art Unit 1642

sjh